

Support for new claim 14 dependent on claim 8, can be found at page 6,
lines 11-15.

In the above Office Action, the Examiner rejected claims 1-8 and 10-13 under 35 U.S.C. § 103(a) for being obvious over Gray. The withdrawal of the rejection of most of these claims for being anticipated by Gray in the Office Action of April 9, 2003, because Gray does not disclose microspheres in the shape of a sphere as claimed is appreciated. However, for the following reasons, it is believed applicants' invention is not obvious in view of Gray either.

Applicants' invention as set forth in main claim 1 relates to a radioactive microsphere comprising not less than 99% by weight of a crystal of an oxide of yttrium which contains 47% by weight or more of radioactive yttrium, and the balance of inevitable impurities, wherein the microsphere is in the shape of a sphere

The invention also relates to a method for making the microspheres comprising preparing a microsphere having not less than 99% by weight of a crystal of an oxide of yttrium which contains 47% by weight or more of non-radioactive yttrium, and the balance of inevitable impurities through melting of a starting material wherein the microsphere is formed into a sphere, followed by irradiating with an effective dosage of slow neutrons to turn non-radioactive yttrium into a radioactive element. Preferably the starting material is an oxide powder containing yttrium, or yttrium and phosphorous.

The claimed radioactive microspheres are excellent in chemical durability and contain a high concentration of radioactive elements that emit radiation for a long period of time. Consequently, they are useful as a medical material for treating tumors by direct irradiation of radiation by embedding the microspheres in the vicinity of the

tumors. Moreover, being in the shape of a sphere they are particularly suitable for use with a catheter for injecting the radioactive microspheres into a patient's body.

As pointed out by the Examiner, Gray discloses radioactive microspheres having a diameter of 5 to 200 microns wherein the microsphere is made of 99.99% pure yttria. The Examiner also acknowledges that the microspheres are not in the shape of a sphere, as claimed, but rather are hollow objects of an irregular shape as described, for example, in column 1, lines 8-10 as "hollow or cup-shaped."

However, the Examiner believes that the shape of the microspheres is a design choice and that it would be obvious to optimize the shape of Gray's microspheres (i.e., to make them a sphere) "to enhance its clinical efficiency." On the contrary, it is submitted that the only suggestion to do so comes from a reading of applicants' specification and not from anything taught by this reference.

Not only did Gray specifically describe his microspheres as being hollow or cup-shaped, he also claimed them in this form. Consequently, it was a specific requirement of his invention that they be in this shape. This can be seen, for example, with reference to column 1, lines 16-20 where patentee states that the radioactive microspheres "are designed to be administered into the arterial blood supply of the organ to be tested, whereby they become entrapped in the small blood vessels of the target organ and irradiate it." Emphasis added. In other words, the microspheres are specifically "designed" to be "entrapped." That is why they are hollow or cup-shaped. If they were truly round as a sphere they would not become entrapped.

How then would this convey to one skilled in the art that they could, for example, be round; particularly since this would be contrary to the express teachings of the reference? As noted in M.P.E.P. §2143.01 page 2100-127 of the 8th edition:

If [the] proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984).

If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious. *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959).

Modifying Gray's microspheres to be spherical would clearly render them unsatisfactory for their intended purpose.

This is further supported by the discussion in Gray in column 2, lines 20-33 where he argues that "if the microspheres ... are too dense or heavy, then they will not distribute evenly in the target organ." Obviously microspheres in the shape of a sphere would be more "dense or heavy" than hollow or cup-shaped microspheres.

It is to be appreciated that applicants' microspheres are to be used with catheters for injecting them into the body. See page 1, line 19 to page 2, line 1 of the specification. Gray does not suggest the need or ability of carrying his microspheres through a catheter.

In the clinical application of the kind of radioactive microspheres of this invention to treat cancer, the microspheres must be smoothly carried through a catheter to the affected region without stagnation in the catheter. For this purpose, sphericity of the microspheres must be high. The microspheres of the present invention are more

more radioactivity can be obtained with a smaller amount of microspheres according to the present invention. The present inventors found that even heavy microspheres consisting of essentially yttria can be distributed evenly when they are suspended in the heavy fluid for angiography.

Accordingly, it is submitted that the noted claims cannot be considered *prima facie* obvious in view of Gray alone, and its withdrawal as a ground of rejection of the claims is requested.

The Examiner also rejected claims 1-8 and 10-13 under 35 U.S.C. § 103(a) for being obvious over Gray in view of Day. In making this rejection, the Examiner, in essence, is maintaining that it would be obvious to substitute the spherical shape of the microspheres of Day for the shape of the microspheres of Gray.

On the contrary, it is submitted that the claims are not obvious over the combination of Gray and Day for all of the above reasons; particularly since such a substitution would "change the principle of operation of the prior art invention being modified" (i.e., Gray) M.P.E.P. §2143.01.

Moreover, in column 3, lines 8-22 of Gray, the patentee specifically teaches against using the solid glass spheres of Day maintaining that they are too heavy because they have "a higher specific gravity than is desirable." In this discussion, the Gray refers to International Patent Publication No. WO86/03124. Enclosed for the Examiner's interest is a copy of the abstract of that publication. Under "priority number" is reference to U.S. Serial No. 673,123 filed November 19, 1984. It can be seen from Day that this is the parent application of the Day reference, it merely being a

cited in the Information Disclosure Statement filed September 10, 2001. Consequently, Gray specifically teaches against making the exact modification thereof proposed by the Examiner. As a result, none of applicants' claims, either the product or method claims, can be considered *prima facie* obvious over the combination of Gray and Day.

In the Office Action on page 3, lines 2 and 3, the Examiner makes reference to "Huang US Patent 5,073,404." However, there is no discussion of this reference, and it is not cited in the Form PTO-892 attached to this Office Action nor in the Office Action of April 9, 2003.

Huang relates to a silica coating composition, so it is believed it was intended to be applied to claims like claims 6 and 12. Regardless of whether or not Huang teaches or suggests what is set forth in these claims, it is submitted the reference fails to suggest what is missing in the combination of Gray and Day. Accordingly, claims 6 and 12 are patentable over Gray in view of Day and Huang for the same reasons set forth above with respect to claims 1 and 8 from which these claims depend.

In any event, it would be appreciated if the Examiner would cite Huang in a Form PTO-892 in his next communication.

It is believed claims 1-8 and 10-13 are in condition for allowance.

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

PLEASc GRANT ANY EXTENSIONS OF TIME REQUIRED TO ENTER THIS RESPONSE AND CHARGE
ANY ADDITIONAL REQUIRED FEES TO OUR DEPOSIT ACCOUNT 06-0916.

Respectfully submitted,

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Dated: March 24, 2004

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